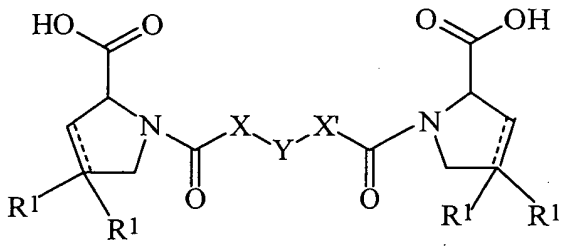
Abstract

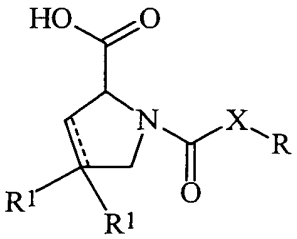
Therapeutic Agent

Agent for the depletion of an unwanted protein population from the plasma of a subject, which agent comprises a plurality of ligands covalently co-linked so as to form a complex with a plurality of the proteins in the presence thereof, wherein at least two of the ligands are the same or different and are capable of being bound by ligand binding sites present on the proteins, wherein the agent is a non-proteinaceous agent other than a D-proline of the formula



I-A

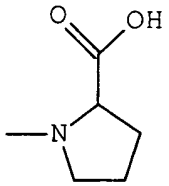
or



I-B

wherein

R is



the group ;

R^1 is hydrogen or halogen;

X is- $(CH_2)_n$-; $-CH(R^2)(CH_2)_n$-; $-CH_2O(CH_2)_n$-; $-CH_2NH$-; benzyl, $-C(R^2)=CH$-; $-CH_2CH(OH)$-; or thiazol-2,5-diyl;

Y is –S-S-; $-(CH_2)_n$-; -O-; -NH-; $-N(R^2)$-; -CH=CH-; -

NHC(O)NH-;-
$N(R^2)C(O)N(R^2)$-; -$N[CH_2C_6H_3(OCH_3)_2]$-; -$N(CH_2C_6H_5)$-;
-$N(CH_2C_6H_5)C(O)N(CH_2C_6H_5)$-; -N(alkoxyalkyl)-;
N(cycloalkyl-methyl)-; 2,6-pyridyl; 2,5-furanyl; 2,5-thienyl; 1,2-cyclohexyl; 1,3-cyclohexyl; 1,4-
cyclohexyl; 1,2-naphthyl; 1,4-naphthyl; 1,5-naphthyl; 1,6-naphthyl;
biphenylen; or 1,2-phenylen,1,3-phenylen and 1,4-phenylen, wherein the phenylen groups are optionally substituted by 1 – 4 substituents, selected from halogen, lower alkyl, lower alkoxy, hydroxy, carboxy, -COO-lower alkyl, nitrilo, 5-tetrazol, (2-carboxylic acid pyrrolidin-1-yl)-2-oxo-ethoxy, N-
hydroxycarbamimidoyl, 5-oxo[1,2,4]oxadiazolyl, 2-oxo-
[1,2,3,5]oxathiadiazolyl, 5-thioxo[1,2,4]oxadiazolyl and 5-tert-butylsulfanyl-[1,2,4]oxadiazolyl;

X' is $-(CH_2)_n$-; -$(CH_2)_nCH(R^2)$-; -$(CH_2)_nOCH_2$-; -$NHCH_2$-;
benzyl, -$CH=C(R^2)$-; -$CH(OH)CH_2$; or thiazol-2,5-diyl;

R^2 is lower alkyl, lower alkoxy or benzyl and

n is 0-3,

or a pharmaceutically acceptable salt or mono- or diester thereof.